

JEMPERLI- dostarlimab injection

GlaxoSmithKline LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use JEMPERLI safely and effectively. See full prescribing information for JEMPERLI.

JEMPERLI (dostarlimab-gxly) injection, for intravenous use

Initial U.S. Approval: 2021

INDICATIONS AND USAGE

JEMPERLI is a programmed death receptor-1 (PD-1)-blocking antibody indicated for the treatment of adult patients with mismatch repair deficient (dMMR) recurrent or advanced endometrial cancer, as determined by an FDA-approved test, that has progressed on or following prior treatment with a platinum-containing regimen. (1)

This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). (1)

DOSAGE AND ADMINISTRATION

- Dose 1 through 4: 500 mg every 3 weeks. (2.2)
- Subsequent dosing beginning 3 weeks after Dose 4 (Dose 5 onwards): 1,000 mg every 6 weeks. (2.2)
- Administer as an intravenous infusion over 30 minutes. (2.2)

DOSAGE FORMS AND STRENGTHS

Injection: 500 mg/10 mL (50 mg/mL) solution in a single-dose vial. (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Immune-mediated adverse reactions can occur in any organ system or tissue, including the following: immune-mediated pneumonitis, immune-mediated colitis, immune-mediated hepatitis, immune-mediated endocrinopathies, immune-mediated nephritis, and immune-mediated dermatologic adverse reactions. Monitor for signs and symptoms of immune-mediated adverse reactions. Evaluate clinical chemistries, including liver and thyroid function, at baseline and periodically during treatment. Withhold or permanently discontinue JEMPERLI and administer corticosteroids based on the severity of reaction. (2.3, 5.1)
- Infusion-related reactions: Interrupt, slow the rate of infusion, or permanently discontinue JEMPERLI based on severity of reaction. (2.3, 5.2)
- Complications of allogeneic HSCT after PD-1/L-1-blocking antibody: Follow patients closely for evidence of transplant-related complications and intervene promptly. (5.3)
- Embryo-fetal toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception. (5.4, 8.1, 8.3)

ADVERSE REACTIONS

Most common adverse reactions ($\geq 20\%$) are fatigue/asthenia, nausea, diarrhea, anemia, and constipation. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

- Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 5/2020

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

- 2.1 Patient Selection
- 2.2 Recommended Dosage
- 2.3 Dosage Modifications for Adverse Reactions
- 2.4 Preparation and Administration

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

- 5.1 Immune-Mediated Adverse Reactions
- 5.2 Infusion-Related Reactions
- 5.3 Complications of Allogeneic HSCT after PD-1/PD-L1-Blocking Antibody
- 5.4 Embryo-Fetal Toxicity

6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience
- 6.2 Immunogenicity

8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.2 Lactation
- 8.3 Females and Males of Reproductive Potential
- 8.4 Pediatric Use
- 8.5 Geriatric Use

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
- 13.2 Animal Toxicology and/or Pharmacology

14 CLINICAL STUDIES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

JEMPERLI is indicated for the treatment of adult patients with mismatch repair deficient (dMMR) recurrent or advanced endometrial cancer (EC), as determined by an FDA-approved test, that has progressed on or following prior treatment with a platinum-containing regimen [see *Dosage and Administration* (2.1)].

This indication is approved under accelerated approval based on tumor response rate and durability of response [see *Clinical Studies* (14)]. Continued approval for this

indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

2 DOSAGE AND ADMINISTRATION

2.1 Patient Selection

Mismatch Repair Deficient (dMMR) Advanced Endometrial Cancer

Select patients with recurrent or advanced endometrial cancer (EC) that has progressed on or following prior treatment with a platinum-containing regimen for treatment with JEMPERLI based on the presence of dMMR in tumor specimens [see *Clinical Studies (14)*]. Information on FDA-approved tests for the detection of dMMR status is available at <http://www.fda.gov/CompanionDiagnostics>.

2.2 Recommended Dosage

The recommended dosage of JEMPERLI is:

- Dose 1 through Dose 4: 500 mg every 3 weeks
- Subsequent dosing beginning 3 weeks after Dose 4 (Dose 5 onwards): 1,000 mg every 6 weeks

Administer JEMPERLI as an intravenous infusion over 30 minutes. Treat patients until disease progression or unacceptable toxicity.

2.3 Dosage Modifications for Adverse Reactions

No dose reductions of JEMPERLI are recommended. In general, withhold JEMPERLI for severe (Grade 3) immune-mediated adverse reactions. Permanently discontinue JEMPERLI for life-threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone equivalent per day within 12 weeks of initiating steroids.

Dosage modifications for JEMPERLI for adverse reactions that require management different from these general guidelines are summarized in Table 1.

Table 1. Recommended Dosage Modifications for Adverse Reactions

Adverse Reaction	Severity ^a	Dosage Modifications
Immune-Mediated Adverse Reactions [see <i>Warnings and Precautions (5.1)</i>]		
Pneumonitis	Grade 2	Withhold ^b
	Grade 3 or 4 or recurrent Grade 2	Permanently discontinue
Colitis	Grade 2 or 3	Withhold ^b
	Grade 4	Permanently discontinue
Hepatitis with no tumor involvement of the liver	AST or ALT increases to more than 3 and up to 8 times ULN or Total bilirubin increases to	Withhold ^b

	more than 1.5 and up to 3 times the ULN	
	AST or ALT increases to more than 8 times the ULN or Total bilirubin increases to more than 3 times the ULN	Permanently discontinue
Hepatitis with tumor involvement of the liver ^c	Baseline AST or ALT is more than 1 and up to 3 times ULN and increases to more than 5 and up to 10 times ULN or Baseline AST or ALT is more than 3 and up to 5 times ULN and increases to more than 8 and up to 10 times ULN	Withhold ^b
	AST or ALT increases to more than 10 times ULN or Total bilirubin increases to more than 3 times ULN	Permanently discontinue
Endocrinopathies	Grade 2, 3, or 4	Withhold if not clinically stable ^b
Nephritis with renal dysfunction	Grade 2 or 3 increased blood creatinine	Withhold ^b
	Grade 4 increased blood creatinine	Permanently discontinue
Exfoliative dermatologic conditions	Suspected SJS, TEN, or DRESS	Withhold ^b
	Confirmed SJS, TEN, or DRESS	Permanently discontinue
Myocarditis	Grade 2, 3, or 4	Permanently discontinue
Neurological toxicities	Grade 2	Withhold ^b
	Grade 3 or 4	Permanently discontinue
Other Adverse Reactions		
Infusion-related reactions [see <i>Warnings and Precautions</i> (5.2)]	Grade 1 or 2	Interrupt or slow the rate of infusion
	Grade 3 or 4	Permanently discontinue

AST = aspartate aminotransferase, ALT = alanine aminotransferase, ULN = upper limit of normal, SJS = Stevens-Johnson syndrome, TEN = toxic epidermal necrolysis, DRESS = drug rash with eosinophilia and systemic symptoms.

^a Based on National Cancer Institute Common Terminology Criteria for Adverse Events, Version 4.0.

^b Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg/day (or equivalent) within 12 weeks of initiating steroids.

^c If AST and ALT are less than or equal to ULN at baseline in patients with liver

involvement, withhold or permanently discontinue JEMPERLI based on recommendations for hepatitis with no liver involvement.

2.4 Preparation and Administration

Preparation for Intravenous Infusion

- Visually inspect the solution for particulate matter and discoloration. The solution is clear to slightly opalescent, colorless to yellow. Discard the vial if visible particles are observed.
- Do not shake.
- For the 500-mg dose, withdraw 10 mL of JEMPERLI from a vial using a disposable sterile syringe made of polypropylene and dilute into an intravenous infusion bag containing 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP to a final concentration between 2 to 10 mg/mL (maximum 250 mL). JEMPERLI is compatible with an infusion bag made of polyolefine, ethylene vinyl acetate, or polyvinyl chloride with DEHP.
- For the 1,000-mg dose, withdraw 10 mL from each of 2 vials (withdraw 20 mL total) and dilute into an intravenous bag containing 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP to a final concentration between 4 to 10 mg/mL (maximum 250 mL).
- Mix diluted solution by gentle inversion. Do not shake.
- Discard any unused portion left in the vial.

Storage of Infusion Solution

Store in the original carton until time of preparation in order to protect from light. The prepared dose may be stored either:

- At room temperature for no more than 6 hours from the time of preparation until the end of infusion.
- Under refrigeration at 2°C to 8°C (36°F to 46°F) for no more than 24 hours from time of preparation until end of infusion. If refrigerated, allow the diluted solution to come to room temperature prior to administration.

Discard after 6 hours at room temperature or after 24 hours under refrigeration.

Do not freeze.

Administration

Administer infusion solution intravenously over 30 minutes through an intravenous line using tubing made of polyvinyl chloride or platinum cured silicon; fittings made of polyvinyl chloride or polycarbonate; and a sterile, non-pyrogenic, low-protein binding, 0.2-micron, in-line or add-on filter.

JEMPERLI must not be administered as an intravenous push or bolus injection. Do not co-administer other drugs through the same infusion line.

3 DOSAGE FORMS AND STRENGTHS

Injection: 500 mg/10 mL (50 mg/mL) clear to slightly opalescent, colorless to yellow solution in a single-dose vial for intravenous infusion after dilution.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Immune-Mediated Adverse Reactions

JEMPERLI is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death receptor-1 (PD-1) or PD-ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance, and inducing immune-mediated adverse reactions. Important immune-mediated adverse reactions listed in WARNINGS AND PRECAUTIONS may not include all possible severe and fatal immune-mediated reactions.

Immune-mediated adverse reactions, which can be severe or fatal, can occur in any organ system or tissue. Immune-mediated adverse reactions can occur at any time after starting a PD-1/PD-L1-blocking antibody. While immune-mediated adverse reactions usually manifest during treatment with PD-1/PD-L1-blocking antibodies, they can also manifest after discontinuation of PD-1/PD-L1-blocking antibodies.

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1-blocking antibodies. Monitor closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function tests at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

Withhold or permanently discontinue depending on severity [see *Dosage and Administration* (2.3)]. In general, if JEMPERLI requires interruption or discontinuation, administer systemic corticosteroids (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reaction is not controlled with corticosteroids.

Toxicity management guidelines for adverse reactions that do not necessarily require systemic steroids (e.g., endocrinopathies, dermatologic reactions) are discussed below.

Immune-Mediated Pneumonitis

JEMPERLI can cause immune-mediated pneumonitis, which can be fatal. The incidence of pneumonitis in patients receiving PD-1/PD-L1 inhibitors, including JEMPERLI, may be increased in patients who have received prior thoracic radiation.

Immune-mediated pneumonitis occurred in 1.1% (5/444) of patients receiving JEMPERLI, including Grade 2 (0.9%) and Grade 3 (0.2%) pneumonitis. Pneumonitis led to discontinuation of JEMPERLI in 0.7% patients.

Systemic corticosteroids were required in all patients with pneumonitis. Pneumonitis

resolved in 80% of the 5 patients. Three patients reinitiated JEMPERLI after symptom improvement; of these 33% had recurrence of pneumonitis.

Immune-Mediated Colitis

JEMPERLI can cause immune-mediated colitis. Cytomegalovirus infection/reactivation have occurred in patients with corticosteroid-refractory immune-mediated colitis treated with PD-1/PD-L1-blocking antibodies. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies.

Immune-mediated colitis occurred in 1.4% (6/444) of patients receiving JEMPERLI, including Grade 3 (0.7%) and Grade 2 (0.7%) adverse reactions. Colitis did not lead to discontinuation of JEMPERLI in any patients.

Systemic corticosteroids were required in 17% (1/6) of patients with colitis. Colitis resolved in 50% of the 6 patients. Of the 2 patients in whom JEMPERLI was withheld for colitis, both reinitiated JEMPERLI.

Immune-Mediated Hepatitis

JEMPERLI can cause immune-mediated hepatitis, which can be fatal.

Immune-mediated hepatitis occurred in 0.2% (1/444) of patients receiving JEMPERLI, which was Grade 3. Systemic corticosteroids were required and the event resolved.

Immune-Mediated Endocrinopathies

Adrenal Insufficiency: JEMPERLI can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment per institutional guidelines, including hormone replacement as clinically indicated. Withhold JEMPERLI if not clinically stable [see *Dosage and Administration* (2.3)].

Adrenal insufficiency occurred in 0.9% (4/444) patients receiving JEMPERLI, including Grade 3 (0.5%) and Grade 2 (0.5%). Adrenal insufficiency resulted in discontinuation in 1 (0.2%) patient and resolved in 25% of the 4 patients.

Hypophysitis: JEMPERLI can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field cuts. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as clinically indicated. Withhold JEMPERLI if not clinically stable [see *Dosage and Administration* (2.3)].

Thyroid Disorders: JEMPERLI can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement or medical management of hyperthyroidism as clinically indicated. Withhold JEMPERLI if not clinically stable [see *Dosage and Administration* (2.3)].

Thyroiditis: Thyroiditis occurred in 0.5% (2/444) of patients receiving JEMPERLI; both were Grade 2. Neither event of thyroiditis resolved; there were no discontinuations of JEMPERLI due to thyroiditis.

Hypothyroidism: Hypothyroidism occurred in 5.6% (25/444) of patients receiving JEMPERLI, all of which were Grade 2. Hypothyroidism did not lead to discontinuation of JEMPERLI and resolved in 40% of the 25 patients. Systemic corticosteroids were not required for any of the 25 patients with hypothyroidism.

Hyperthyroidism: Hyperthyroidism occurred in 1.8% (8/444) of patients receiving JEMPERLI, including Grade 2 (1.6%) and Grade 3 (0.2%). Hyperthyroidism did not lead to discontinuation of JEMPERLI and resolved in 63% of the 8 patients. Systemic corticosteroids were not required for any of the 8 patients with hyperthyroidism.

Type 1 Diabetes Mellitus, Which Can Present with Diabetic Ketoacidosis: JEMPERLI can cause type 1 diabetes mellitus, which can present with diabetic ketoacidosis. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold or permanently discontinue JEMPERLI depending on severity [see *Dosage and Administration* (2.3)].

Immune-Mediated Nephritis with Renal Dysfunction

JEMPERLI can cause immune-mediated nephritis, which can be fatal. Nephritis occurred in 0.5% (2/444) of patients receiving JEMPERLI; both were Grade 2. Nephritis did not lead to discontinuation of JEMPERLI and resolved in both patients. Systemic corticosteroids were required in 1 of the 2 patients experiencing nephritis.

Immune-Mediated Dermatologic Adverse Reactions

JEMPERLI can cause immune-mediated rash or dermatitis. Bullous and exfoliative dermatitis, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug rash with eosinophilia and systemic symptoms (DRESS), have occurred with PD-1/PD-L1-blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-bullous/exfoliative rashes. Withhold or permanently discontinue JEMPERLI depending on severity [see *Dosage and Administration* (2.3)].

Other Immune-Mediated Adverse Reactions

The following clinically significant immune-mediated adverse reactions occurred in <1% of the 444 patients treated with JEMPERLI or were reported with the use of other PD-1/PD-L1-blocking antibodies. Severe or fatal cases have been reported for some of these adverse reactions.

Nervous System: Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis, Guillain-Barre syndrome, nerve paresis, autoimmune neuropathy.

Cardiac/Vascular: Myocarditis, pericarditis, vasculitis.

Ocular: Uveitis, iritis, other ocular inflammatory toxicities. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss.

Gastrointestinal: Pancreatitis, including increases in serum amylase and lipase levels, gastritis, duodenitis.

Musculoskeletal and Connective Tissue: Myositis/polymyositis, rhabdomyolysis and associated sequelae including renal failure, arthritis, polymyalgia rheumatica.

Endocrine: Hypoparathyroidism.

Other (Hematologic/Immune): Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing

lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenia, solid organ transplant rejection.

5.2 Infusion-Related Reactions

Severe or life-threatening infusion-related reactions have been reported with PD-1/PD-L1-blocking antibodies. Severe infusion-related reactions (Grade 3) occurred in 0.2% (1/444) of patients receiving JEMPERLI. All patients recovered from the infusion-related reactions.

Monitor patients for signs and symptoms of infusion-related reactions. Interrupt or slow the rate of infusion or permanently discontinue JEMPERLI based on severity of reaction [*see Dosage and Administration (2.3)*].

5.3 Complications of Allogeneic HSCT after PD-1/PD-L1-Blocking Antibody

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/PD-L1-blocking antibody. Transplant-related complications include hyperacute graft-versus-host disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/PD-L1 blockade and allogeneic HSCT.

Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1-blocking antibody prior to or after an allogeneic HSCT.

5.4 Embryo-Fetal Toxicity

Based on its mechanism of action, JEMPERLI can cause fetal harm when administered to a pregnant woman. Animal studies have demonstrated that inhibition of the PD-1/PD-L1 pathway can lead to increased risk of immune-mediated rejection of the developing fetus, resulting in fetal death. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with JEMPERLI and for 4 months after the last dose [*see Use in Specific Populations (8.1, 8.3)*].

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Immune-mediated adverse reactions [*see Warnings and Precautions (5.1)*]
- Infusion-related reactions [*see Warnings and Precautions (5.2)*]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The pooled safety population described in WARNINGS AND PRECAUTIONS reflects

exposure to JEMPERLI in 444 patients with advanced or recurrent solid tumors in the open-label, multicohort GARNET study including 268 patients with EC and 176 patients with other solid tumors. JEMPERLI as a single agent was administered intravenously at doses of 500 mg every 3 weeks for 4 doses followed by 1,000 mg every 6 weeks until disease progression or unacceptable toxicity. Among the 444 patients, 38% were exposed for ≥ 6 months and 12% were exposed for ≥ 1 year.

Mismatch Repair Deficient (dMMR) Endometrial Cancer

The safety of JEMPERLI was evaluated in the GARNET trial in 104 patients with advanced or recurrent dMMR EC who received at least one dose of JEMPERLI [see *Clinical Studies (14)*]. Patients received JEMPERLI 500 mg every 3 weeks for 4 doses followed by 1,000 mg every 6 weeks as an intravenous infusion until disease progression or unacceptable toxicity. Among patients receiving JEMPERLI, 47% were exposed for 6 months or longer and 20% were exposed for >1 year.

Serious adverse reactions occurred in 34% of patients receiving JEMPERLI. Serious adverse reactions in $>2\%$ of patients included sepsis (2.9%), acute kidney injury (2.9%), urinary tract infection (2.9%), abdominal pain (2.9%), and pyrexia (2.9%).

JEMPERLI was permanently discontinued due to adverse reactions in 5 (4.8%) patients, including transaminases increased, sepsis, bronchitis, and pneumonitis. Dosage interruptions due to an adverse reaction occurred in 23% of patients who received JEMPERLI. Adverse reactions that required dosage interruption in $\geq 1\%$ of patients who received JEMPERLI were anemia, diarrhea, increased lipase, and pyrexia.

The most common adverse reactions ($\geq 20\%$) were fatigue/asthenia, nausea, diarrhea, anemia, and constipation. The most common Grade 3 or 4 adverse reactions ($\geq 2\%$) were anemia and transaminases increased.

Table 2 summarizes the adverse reactions that occurred in $\geq 10\%$ of patients with dMMR EC on JEMPERLI in the GARNET study.

Table 2. Adverse Reactions ($\geq 10\%$) in Patients with dMMR Endometrial Cancer who Received JEMPERLI in GARNET

Adverse Reaction	JEMPERLI N = 104	
	All Grades %	Grade 3 or 4 %
Blood and Lymphatic System		
Anemia ^a	24	13
Gastrointestinal		
Nausea	30	0
Diarrhea	26	1.9
Constipation	20	0.9
Vomiting	18	0
General and Administration Site		
Fatigue ^b	48	1
Infections		
Urinary tract infection	13	1.9

Metabolism and Nutrition Decreased appetite	14	0
Musculoskeletal and Connective Tissue Myalgia	12	0
Respiratory, Thoracic, and Mediastinal Cough	14	0
Skin and Subcutaneous Tissue Pruritus	14	1

Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.03.

^a Includes anemia, hemoglobin decreased, iron deficiency, and iron deficiency anemia.

^b Includes fatigue and asthenia.

Table 3 summarizes Grade 3 or 4 laboratory abnormalities worsening from baseline in $\geq 1\%$ of patients with dMMR EC on JEMPERLI in the GARNET study.

Table 3. Laboratory Abnormalities that Worsened from Baseline to Grade 3 or 4 Occurring in $\geq 1\%$ of Patients with dMMR EC Receiving JEMPERLI in GARNET

Laboratory Test	JEMPERLI N = 104	
	All Grades ^a %	Grade 3 or 4 ^a %
Hematology		
Lymphopenia	37	9
Leukopenia	21	2.9
Chemistry		
Hypoalbuminemia	30	2.9
Increased alkaline phosphatase	25	2.9
Increased creatinine	27	2.9
Hyponatremia	26	4.8
Hypercalcemia	15	1.9
Increased alanine aminotransferase	15	2.9
Hypokalemia	15	1.9
Increased aspartate aminotransferase	16	1.9

dMMR EC = Mismatch Repair Deficient Endometrial Cancer.

^a Consists of new onset of laboratory abnormality or worsening of baseline laboratory abnormality.

6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to dostarlimab-gxly in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

The immunogenicity of dostarlimab was evaluated in the GARNET study. The treatment-emergent anti-drug antibodies (ADAs) against dostarlimab-gxly were detected in 2.5% of 315 patients treated with dostarlimab-gxly at the recommended therapeutic dose. Neutralizing antibodies were detected in 1.3% of patients. Because of the small number of patients who developed ADAs, the impact of immunogenicity on the efficacy and safety of dostarlimab-gxly is inconclusive.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on its mechanism of action, JEMPERLI can cause fetal harm when administered to a pregnant woman [see *Clinical Pharmacology* (12.1)]. There are no available data on the use of JEMPERLI in pregnant women. Animal studies have demonstrated that inhibition of the PD-1/PD-L1 pathway can lead to increased risk of immune-mediated rejection of the developing fetus resulting in fetal death (see *Data*). Human IgG4 immunoglobulins (IgG4) are known to cross the placental barrier; therefore, dostarlimab-gxly has the potential to be transmitted from the mother to the developing fetus. Advise women of the potential risk to a fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data: Animal reproduction studies have not been conducted with JEMPERLI to evaluate its effect on reproduction and fetal development. A central function of the PD-1/PD-L1 pathway is to preserve pregnancy by maintaining maternal immune tolerance to the fetus. In murine models of pregnancy, blockade of PD-L1 signaling has been shown to disrupt tolerance to the fetus and to result in an increase in fetal loss; therefore, potential risks of administering JEMPERLI during pregnancy include increased rates of abortion or stillbirth. As reported in the literature, there were no malformations related to the blockade of PD-1/PD-L1 signaling in the offspring of these animals; however, immune-mediated disorders occurred in PD-1 and PD-L1 knockout mice. Based on its mechanism of action, fetal exposure to dostarlimab-gxly may increase the risk of developing immune-mediated disorders or altering the normal immune response.

8.2 Lactation

Risk Summary

There is no information regarding the presence of dostarlimab-gxly in human milk or its effects on the breastfed child or on milk production. Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment and for 4 months after the last dose of JEMPERLI.

8.3 Females and Males of Reproductive Potential

JEMPERLI can cause fetal harm when administered to a pregnant woman [see *Use in Specific Populations* (8.1)].

Pregnancy Testing

Verify pregnancy status in females of reproductive potential prior to initiating JEMPERLI [see *Use in Specific Populations* (8.1)].

Contraception

Females: Advise females of reproductive potential to use effective contraception during treatment with JEMPERLI and for 4 months after the last dose.

8.4 Pediatric Use

The safety and efficacy of JEMPERLI have not been established in pediatric patients.

8.5 Geriatric Use

Of the 444 patients treated with JEMPERLI, 49% were younger than 65 years, 39% were aged 65 through 75 years, and 12% were 75 years or older. No overall differences in safety or effectiveness were observed between these patients and younger patients.

11 DESCRIPTION

Dostarlimab-gxly is a programmed death receptor-1 (PD-1)-blocking IgG₄ humanized monoclonal antibody. Dostarlimab-gxly is produced in Chinese hamster ovary cells and has a calculated molecular weight of about 144 kDa.

JEMPERLI (dostarlimab-gxly) injection is a sterile, clear to slightly opalescent, colorless to yellow solution essentially free from visible particles. It is supplied as single-dose vials.

Each vial contains 500 mg of JEMPERLI in 10 mL of solution. Each mL of solution contains 50 mg of dostarlimab-gxly, citric acid monohydrate (0.48 mg), L-arginine hydrochloride (21.07 mg), polysorbate 80 (0.2 mg), sodium chloride (1.81 mg), trisodium citrate dihydrate (6.68 mg), and Water for Injection, USP.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Binding of the PD-1 ligands, PD-L1 and PD-L2, to the PD-1 receptor found on T cells inhibits T-cell proliferation and cytokine production. Upregulation of PD-1 ligands occurs in some tumors, and signaling through this pathway can contribute to inhibition of active T-cell immune surveillance of tumors. Dostarlimab-gxly is a humanized monoclonal antibody of the IgG₄ isotype that binds to the PD-1 receptor and blocks its interaction

with PD-L1 and PD-L2, releasing PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response. In syngeneic mouse tumor models, blocking PD-1 activity resulted in decreased tumor growth.

12.2 Pharmacodynamics

Dostarlimab-gxly exposure-response relationships have not been fully characterized. Dostarlimab-gxly provides sustained target engagement as measured by PD-1 binding and stimulation of IL-2 production throughout the dosing interval at the recommended dose.

12.3 Pharmacokinetics

The pharmacokinetics of dostarlimab-gxly were evaluated in patients with various solid tumors, including 150 patients with EC. Mean C_{max} , AUC_{0-inf} , and AUC_{0-tau} increased proportionally over the dose range of 1.0 to 10 mg/kg. The Cycle 1 mean (coefficient of variation [%CV]) C_{max} and AUC_{0-tau} of dostarlimab-gxly are 171 mcg/mL (20%) and 35,730 mcg*h/mL (20%) at the dose of 500 mg once every 3 weeks and 309 mcg/mL (31%) and 95,820 mcg*h/mL (29%) at the dose of 1,000 mg every 6 weeks, respectively.

Distribution

The mean (%CV) volume of distribution of dostarlimab-gxly at steady state is 5.3 L (12%).

Elimination

The mean terminal elimination half-life of dostarlimab-gxly is 25.4 days and its mean (%CV) clearance is 0.007 L/h (31%) at steady state.

Metabolism: Dostarlimab-gxly is expected to be metabolized into small peptides and amino acids by catabolic pathways.

Specific Populations

No clinically significant differences in the pharmacokinetics of dostarlimab-gxly were observed based on age (24 to 86 years), sex (79% female), race/ethnicity (78% White, 2% Asian, 4% African American, and 16% other), tumor types, and renal impairment based on the estimated creatinine clearance (CL_{CR} mL/min) (normal: $CL_{CR} \geq 90$ mL/min, $n = 173$; mild: $CL_{CR} = 60-89$ mL/min, $n = 210$; moderate: $CL_{CR} = 30-59$ mL/min, $n = 90$; severe: $CL_{CR} = 15-29$ mL/min, $n = 3$; and end-stage renal disease: $CL_{CR} < 15$ mL/min, $n = 1$) and hepatic impairment as measured by total bilirubin (TB) and aspartate aminotransferase (AST) (normal: TB and AST less than or equal to upper limit of normal [ULN], $n = 425$; mild: $TB > ULN$ to $1.5 ULN$ or $AST > ULN$, $n = 48$; and moderate: $TB > 1.5-3 ULN$, any AST, $n = 4$).

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No studies have been performed to assess the potential of dostarlimab-gxly for carcinogenicity or genotoxicity.

Fertility studies have not been conducted with dostarlimab-gxly. In 1- and 3-month repeat-dose toxicology studies in monkeys, there were no notable effects in the male and female reproductive organs; however, many animals in these studies were not sexually mature.

13.2 Animal Toxicology and/or Pharmacology

In animal models, inhibition of PD-L1/PD-1 signaling increased the severity of some infections and enhanced inflammatory responses. Mycobacterium tuberculosis-infected PD-1 knockout mice exhibit markedly decreased survival compared with wild-type controls, which correlated with increased bacterial proliferation and inflammatory responses in these animals. PD-L1 and PD-1 knockout mice and mice receiving PD-L1-blocking antibody have also shown decreased survival following infection with lymphocytic choriomeningitis virus.

14 CLINICAL STUDIES

The efficacy of JEMPERLI was evaluated in the GARNET study (NCT02715284), a multicenter, multicohort, open-label study conducted in patients with advanced solid tumors. The efficacy population consisted of a cohort of 71 patients with mismatch repair deficient (dMMR) recurrent or advanced EC who had progressed on or after treatment with a platinum-containing regimen. Patients with prior treatment with PD-1/PD-L1-blocking antibodies or other immune checkpoint inhibitor therapy and patients with autoimmune disease that required systemic therapy with immunosuppressant agents within 2 years were excluded from the study.

Patients received JEMPERLI 500 mg intravenously every 3 weeks for 4 doses followed by 1,000 mg intravenously every 6 weeks. Treatment continued until disease progression or unacceptable toxicity. The major efficacy outcome measures were Overall Response Rate (ORR) and Duration of Response (DOR) as assessed by blinded independent central review (BICR) according to the Response Evaluation Criteria in Solid Tumors (RECIST) v 1.1.

The baseline characteristics were: median age 64 years (49% aged 65 years or older); 82% White, 3% Asian, 1% Black; and Eastern Cooperative Oncology Group Performance Status 0 (32%) or 1 (68%).

At time of study entry, 66% of the patients with dMMR EC had International Federation of Gynecology and Obstetrics (FIGO) Stage IV disease. The most common histology seen was endometrioid carcinoma type 1 (70%), followed by serous (6%) and mixed and undifferentiated (2.8% each).

All patients with dMMR EC had received prior anticancer treatment, with 90% of patients receiving prior anticancer surgery and 79% receiving prior anticancer radiotherapy. Approximately 40% had 2 lines or more of prior anticancer treatment. Approximately 11% of patients had received 3 regimens and 4% had received 4 or more prior regimens.

The dMMR tumor status was retrospectively confirmed using the VENTANA MMR RxDx Panel assay.

Efficacy results are presented in Table 4.

Table 4. Efficacy Results in GARNET dMMR Endometrial Cancer Population

Endpoint	JEMPERLI N = 71
Confirmed Overall Response Rate	
ORR	42.3%
(95% CI)	(30.6, 54.6)
Complete response rate	12.7%
Partial response rate	29.6%
Duration of Response	
Median in months (range) ^a	Not reached (2.6, 22.4+)
Patients with duration ≥6 months	93.3%

CI = Confidence interval, + = ongoing at last assessment.

^a Median follow-up for DOR was 14.1 months, measured from time of first response.

16 HOW SUPPLIED/STORAGE AND HANDLING

JEMPERLI (dostarlimab-gxly) injection is a clear to slightly opalescent, colorless to yellow solution supplied in a carton containing one 500 mg/10 mL (50 mg/mL), single-dose vial (NDC 0173-0898-03).

Store vial refrigerated at 2°C to 8°C (36°F to 46°F) in original carton to protect from light. Do not freeze or shake.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Immune-Mediated Adverse Reactions

Inform patients of the risk of immune-mediated adverse reactions that may be severe or fatal, may occur after discontinuation of treatment, and may require corticosteroid or other treatment and interruption or discontinuation of JEMPERLI. These reactions may include:

- Pneumonitis: Advise patients to contact their healthcare provider immediately for new or worsening cough, chest pain, or shortness of breath [see *Warnings and Precautions* (5.1)].
- Colitis: Advise patients to contact their healthcare provider immediately for diarrhea or severe abdominal pain [see *Warnings and Precautions* (5.1)].
- Hepatitis: Advise patients to contact their healthcare provider immediately for jaundice, severe nausea or vomiting, or easy bruising or bleeding [see *Warnings and Precautions* (5.1)].
- Immune-mediated endocrinopathies: Advise patients to contact their healthcare provider immediately for signs or symptoms of hypothyroidism, hyperthyroidism, thyroiditis, adrenal insufficiency, hypophysitis, or type 1 diabetes mellitus [see *Warnings and Precautions* (5.1)].
- Nephritis: Advise patients to contact their healthcare provider immediately for signs or symptoms of nephritis [see *Warnings and Precautions* (5.1)].

- Severe skin reactions: Advise patients to contact their healthcare provider immediately for any signs or symptoms of severe skin reactions, SJS, or TEN [see *Warnings and Precautions (5.1)*].
- Other immune-mediated adverse reactions:
 - Advise patients that immune-mediated adverse reactions can occur and may involve any organ system, and to contact their healthcare provider immediately for any new signs or symptoms [see *Warnings and Precautions (5.1)*].

Infusion-Related Reactions

- Advise patients to contact their healthcare provider immediately for signs or symptoms of infusion-related reactions [see *Warnings and Precautions (5.2)*].

Embryo-Fetal Toxicity

- Advise females of reproductive potential of the potential risk to a fetus and to inform their healthcare provider of a known or suspected pregnancy [see *Warnings and Precautions (5.4), Use in Specific Populations (8.1, 8.3)*].
- Advise females of reproductive potential to use effective contraception during treatment with JEMPERLI and for 4 months after the last dose [see *Warnings and Precautions 5.4), Use in Specific Populations (8.1, 8.3)*].

Lactation

- Advise women not to breastfeed during treatment with JEMPERLI and for 4 months after the last dose [see *Use in Specific Populations (8.2)*].

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Philadelphia, PA 19112

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Research Triangle Park, NC 27709

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JMP:1PI

<p style="text-align: center;">MEDICATION GUIDE JEMPERLI (jem-PER-lee) (dostarlimab-gxly) injection</p>
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<p>What is the most important information I should know about JEMPERLI? JEMPERLI is a medicine that may treat certain cancers by working with your immune system. JEMPERLI can cause your immune system to attack normal organs and tissues</p>

in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. These problems may happen anytime during treatment or even after your treatment has ended.

Call or see your healthcare provider right away if you develop any symptoms of the following problems or if these symptoms get worse:

Lung problems (pneumonitis). Symptoms of pneumonitis may include:

Intestinal problems (colitis) that can lead to tears or holes in your intestine.

Signs and symptoms of colitis may include:

Liver problems, including hepatitis. Signs and symptoms of liver problems may include:

Hormone gland problems (especially the adrenal glands, pituitary, thyroid, and pancreas). Signs and symptoms that your hormone glands are not working properly may include:

Kidney problems, including nephritis and kidney failure. Signs of kidney problems may include:

Skin problems. Signs of skin problems may include:

Problems in other organs. Signs and symptoms of these problems may include:

Infusion reactions that can sometimes be severe and life-threatening. Signs and symptoms of infusion reactions may include:

Complications, including graft-versus-host-disease (GVHD), in people who have received a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic). These complications can be severe and can lead to death. These complications may happen if you underwent transplantation either before or after being treated with JEMPERLI. Your healthcare provider will monitor you for the following signs and symptoms: skin rash, liver inflammation, stomach-area (abdominal) pain, and diarrhea.

Getting medical treatment right away may help keep these problems from becoming more serious.

Your healthcare provider will check you for these problems during treatment with JEMPERLI. Your healthcare provider may treat you with corticosteroid or hormone replacement medicines. Your healthcare provider may also need to delay or completely stop treatment with JEMPERLI, if you have severe side effects.

What is JEMPERLI?

JEMPERLI is a prescription medicine used to treat adults with a kind of uterine cancer called endometrial cancer. JEMPERLI may be used when:

- your tumor has been shown by a laboratory test to be mismatch repair deficient (dMMR), **and**
 - your cancer has returned, or it has spread or cannot be removed by surgery (advanced cancer), **and**
 - you have received chemotherapy that contains platinum and it did not work or is no longer working.

It is not known if JEMPERLI is safe and effective in children.

Before you receive JEMPERLI, tell your healthcare provider if you have any medical conditions, including if you:

- have immune system problems.
- have lung or breathing problems.

- are pregnant or plan to become pregnant. JEMPERLI can harm your unborn baby.

Females who are able to become pregnant:

- o Your healthcare provider will do a pregnancy test before you start treatment with JEMPERLI.
- o You should use effective birth control during treatment and for 4 months after your last dose of JEMPERLI. Talk to your healthcare provider about birth control methods that you can use during this time.
- o Tell your healthcare provider right away if you think you may be pregnant or if you become pregnant during treatment with JEMPERLI.
- are breastfeeding or plan to breastfeed. It is not known if JEMPERLI passes into your breast milk. Do not breastfeed during treatment and for 4 months after your last dose of JEMPERLI.

Tell your **healthcare provider about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How will I receive JEMPERLI?

- Your healthcare provider will give you JEMPERLI into your vein through an intravenous (IV) line over 30 minutes.
- JEMPERLI is usually given every 3 weeks for the first 4 doses, and then beginning 3 weeks later, it is usually given every 6 weeks.
- Your healthcare provider will decide how many treatments you need.
- Your healthcare provider will do blood tests to check you for side effects.
- If you miss any appointments, call your healthcare provider as soon as possible to reschedule your appointment.

What are the possible side effects of JEMPERLI?

JEMPERLI can cause serious side effects. See “What is the most important information I should know about JEMPERLI?”

The most common side effects of JEMPERLI include: tiredness and weakness, nausea, diarrhea, low red blood count (anemia), and constipation.

These are not all the possible side effects of JEMPERLI. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of JEMPERLI

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. If you would like more information about JEMPERLI, talk with your healthcare provider. You can ask your healthcare provider for information about JEMPERLI that is written for healthcare professionals.

What are the ingredients in JEMPERLI?

Active ingredient: dostarlimab-gxly

Inactive ingredients: citric acid monohydrate, L-arginine hydrochloride, polysorbate 80, sodium chloride, trisodium citrate dihydrate, and Water for Injection.

Manufactured by: GlaxoSmithKline LLC, Philadelphia, PA 19112

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Distributed by: GlaxoSmithKline, Research Triangle Park, NC 27709

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For more information, call 1-888-825-5249 or go to gsk.com.

This Medication Guide has been approved by the U.S. Food and Drug Administration. Issued: April 2021

PRINCIPAL DISPLAY PANEL

NDC 0173-0898-03

Jemperli

(dostarlimab-gxly) Injection

500 mg/10 mL

(50 mg/mL)

gsk

For Intravenous Infusion after Dilution

Single-Dose Vial

Dosage: See Prescribing Information.

Storage: Refrigerate at 2°C to 8°C (36°F to 46°F) in original carton to protect from light.

Do not freeze or shake.

Discard unused portion.

Do not accept if plastic overseal is missing or not securely fitted.

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Rev. 10/20

PCR-700-13182

NDC 0173-0898-03



Jemperli 

**(dostarlimab-gxly)
Injection**

**500 mg/10 mL
(50 mg/mL)**

**For Intravenous Infusion after
Dilution
Single-Dose Vial**

Rx only

**Dispense the enclosed
Medication Guide to each patient.**

JEMPERLI

dostarlimab injection

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:0173-0898
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
DOSTARLIMAB (UNII: P0GVQ9A4S5) (DOSTARLIMAB - UNII:P0GVQ9A4S5)	DOSTARLIMAB	50 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
CITRIC ACID MONOHYDRATE (UNII: 2968PHW8QP)	
ARGININE HYDROCHLORIDE (UNII: F7LTH1E20Y)	
POLYSORBATE 80 (UNII: 6OZP39ZG8H)	
SODIUM CHLORIDE (UNII: 451W47IQ8X)	
TRISODIUM CITRATE DIHYDRATE (UNII: B22547B95K)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0173-0898-03	1 in 1 CARTON	04/22/2021	
1		10 mL in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA761174	04/22/2021	

Labeler - GlaxoSmithKline LLC (167380711)

Revised: 4/2021

GlaxoSmithKline LLC